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**Tear mucus ferning patterns in the diagnosis and management of dry eye syndrome: A comparison between the ocular surface disease index questionnaire, as a subjective test, and tear mucus ferning patterns, as an objective test**

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## **Abstract**

Dry eye syndrome (DES) is a very common ocular morbidity in the U.S. and eye care professionals should have a deep knowledge of its pathophysiology. No objective tests have been found that correlate well with subjective symptoms. Because of this, we wanted to see if tear mucus ferning patterns (TMFPs) correlated with subjective symptoms as measured with the ocular surface disease index (OSDI) questionnaire. We collected tear samples and got questionnaires filled out from the same participants in October-November and then April-May. When considering both sessions together, 47 out of 55 or 85.45% of our participants had symptoms and 20 of those 47 or 42.55% had an abnormal TMFP. A stronger correlation between an objective test and subjective measurements than any studies we have found. However, in our statistical analysis, the two tests were not predictive of one another (1st session Spearman rho= -0.1392 and 2nd session Spearman rho= +0.2055). The analysis shows that TMFPs are not the test to diagnose DES, but that it is a good objective tool that should be used to assist with diagnosis. It should be noted that abnormal TMFPs are an indication of tear film mucus layer deficiency/ pathology and is only one of many potential causes of DES.

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**TEAR MUCUS FERNING PATTERNS IN THE DIAGNOSIS AND  
MANAGEMENT OF DRY EYE SYNDROME: A COMPARISON  
BETWEEN THE OCULAR SURFACE DISEASE INDEX  
QUESTIONNAIRE, AS A SUBJECTIVE TEST, AND TEAR MUCUS  
FERNING PATTERNS, AS AN OBJECTIVE TEST**

**BY**

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**Advisors:**

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## **BIOGRAPHIES:**

Jeff Mellor is from Utah and comes from a family of seven. He has received a B.S. in Medical Laboratory Science and a minor in chemistry from the University of Utah in May of 2000. He is pursuing a Doctor of Optometry degree (O.D) and an M. Ed. with emphasis in visual function and learning from Pacific University. His goals are to complete an optometry residency and practice optometry in the Salt Lake City, Utah region. He has been strongly supported by his wife through his education and has two children.

Adina Zapodeanu is from Romania. She graduated from medical school and completed residency training in ophthalmology over there. Life brought her to the USA and she considered optometry to be the best option to fulfill her professional career and aspirations. She and her husband have two boys, Stephan and Matthew, both born while attending optometry school. She will graduate from Pacific University in May 2005, with dreams of practicing optometry in the Pacific Northwest.

## **ABSTRACT:**

Dry eye syndrome (DES) is a very common ocular morbidity in the U.S. and eye care professionals should have a deep knowledge of its pathophysiology. No objective tests have been found that correlate well with subjective symptoms. Because of this, we wanted to see if tear mucus fearning patterns (TMFPs) correlated with subjective symptoms as measured with the ocular surface disease index (OSDI) questionnaire.

We collected tear samples and got questionnaires filled out from the same participants in October-November and then April-May. When considering both sessions together, 47 out of 55 or 85.45 % of our participants had symptoms and 20 of those 47 or 42.55% had an abnormal TMFP. A stronger correlation between an objective test and subjective measurements than any studies we have found. However, in our statistical analysis, the two tests were not predictive of one another (1<sup>st</sup> session Spearman rho = -0.1392 and 2<sup>nd</sup> session Spearman rho = +0.2055).

The analysis shows that TMFPs are not the test to diagnose DES, but that it is a good objective tool that should be used to assist with diagnosis. It should be noted that abnormal TMFPs are an indication of tear film mucus layer deficiency/pathology and is only one of many potential causes of DES.

## **ACKNOWLEDGMENTS:**

We, the authors, would like to express our deepest appreciation to Patrick Caroline, and Dr. Peter Berginske for their advice and guidance in this project. They have provided us with valuable insights and direction. We hope that this thesis will be of great use to optometry and other medical professions who have a role in evaluating dry eye syndrome.

We are also very grateful to our families, spouses, and children for the understanding and patience they have shown during the many ours it has taken to complete this study.



## **Introduction**

Dry eye syndrome (DES) is a very common ocular morbidity, affecting over 14 million Americans. It causes ocular discomfort and can interfere with daily function. The total dry eye treatment market was estimated to be over 2.3 billion U.S. dollars in July of 2003 (11). Because it is so common among the US population and there are huge sums of money spent on its treatment the importance of accurate diagnosis could not be over emphasized.

DES can affect the quality of the patients' life. Schiffman & al, demonstrated that the loss of utility due to severe dry eye is similar to that reported for moderate to severe (class III/IV) angina pectoris, and that due to less severe dry eye is greater than that of mild chronic psoriasis (29). Since dry eye disease reduces quality of life, it should be taken seriously by practitioners.

## **Definition**

National Eye Institute/Industry Workshops (December '93, '94) defined DES as "a disorder of the tear film due to tear deficiency or excessive tear evaporation which both can cause damage to the interpalpebral ocular surface and are associated with symptoms of ocular discomfort." (12).

## **Review of Anatomy and Physiology**

The tear film covers the anterior ocular surface of the cornea and conjunctiva. In the traditional model it has a three-layered structure: the outer lipid layer, middle aqueous layer, and the inner mucous layer. Meibomian glands primarily produce the outer lipid layer (0.1 $\mu$ m thick) with secondary production by the glands of Zeiss and Moll. The lacrimal gland and accessory glands of Wolfring and Krause produce the aqueous layer (7  $\mu$ m thick). Conjunctival goblet cells and stratified squamous cells of the cornea and conjunctiva epithelia produce the mucus layer (0.02-0.05  $\mu$ m thick) (7).

The tear film has very important roles in the health and function of ocular surface, they include:

- ◆ Most anterior optical surface of the eye, critical for clear vision
- ◆ Primary source of oxygen for the avascular cornea
- ◆ Lubricates ocular surface

- Flushes away foreign bodies, allergens & pathogens
- Contains antimicrobial proteins like lactoferrin or IgA antibodies to protect against infection

## **Prevalence**

There is no general consensus in the prevalence of DES. For example, Doughty and al showed that in the general population the prevalence of patients with any level of DES is 25% and those with severe symptoms were reported to be 1 in 225 patients (2). Two age groups seem to have the highest prevalence of this condition; they are between 21-30 (38% by Doughty and al) and over 65 (14.6% by Schein & al, 33.7% by Lin & al) (2, 26 & 13). The Salisbury study also showed a prevalence of 14.6% and the Beaver Dam study showed 14.4% in patients 65 and older (27 & 16).

A higher prevalence of DES is associated with the contact lens wear, eyelid abnormalities, first 3-6 months after refractive surgery, allergies, dry mouth, diabetes, arthritis, use of antihistamines or diuretics, and with poorer self-rated health (2, 16 & 15). Also, the prevalence is believed to be higher in females (15). On the other hand, in the Salisbury study, Schein found no association of symptoms or signs with age, sex, or race (26).

A study done in Japan showed that even though the awareness of DES in the general population was high (73%), only a minority of the population (6.8%) learned about DES from their physicians. This study indicates that most knowledge the public has about DES is obtained through the media (30).

## **Pathophysiology**

The two most common types of DES are tear film deficiency and/or tear film evaporation. Causes are unknown (idiopathic) or the result of different ocular or general diseases (3).

Systemic pathologies leading to tear film deficiency are called Sjogren's syndrome; they are usually associated with autoimmune diseases like rheumatoid arthritis, systemic lupus erythematosus, Wegener's granulomatosis, systemic sclerosis, primary billiary cirrhosis, etc.... Ocular pathologies leading to tear film deficiency are called non-Sjogren's syndrome; these include conditions like lacrimal disease, lacrimal obstruction, and reflex tear deficiency (3).

Increased tear film evaporation is caused mainly by local conditions like contact lens use, oil deficiency, meibomian gland dysfunction, lid related abnormalities, blepharitis, and ocular surface changes like in xerophthalmia (3).

## **Clinical Patterns & Diagnostic Methods**

Clinical patterns of the DES vary very widely. There is not a standard patient with DES, but most patients have symptoms, interpalpebral surface damage, tear instability, and tear hyperosmolarity (3).

The general consensus is that DES is a symptom-based condition. Symptoms change throughout the day, suggesting that open-eye conditions affect the progression of symptoms. Typical symptoms are discomfort, burning, soreness, itching, foreign body sensation, grittiness, scratchiness, stinging, dryness, photophobia, ocular fatigue, epiphora, pain, redness and blinking abnormalities. Visual disturbances are often reported due to tear film unevenness, drying and instability. Frequently patients with DES need to blink a few times to see a clear 20/20.

National Eye Institute Workshops in Dry Eyes classification ('94, '95) included ocular surface symptoms as the first criterion for the classification of dry eye and points to the need for a validated DES questionnaire (12).

There is a lack of consensus about which diagnostic tests are effective in diagnosing DES. As we described above there are a wide range of etiologies and great variability of symptoms, so it is difficult to develop a consistent and valid battery of objective tests to diagnose and classify the severity of this disease.

Objective tests utilized to help make the diagnosis of dry eye can be classified into three classes:

1. Slit lamp biomicroscopy with diagnostic dye evaluation tests: fluorescein, rose bengal or lissamine green staining
2. Tear film stability tests: tear film break-up time (TFBUT), non-contact TFBUT, reflective meniscometry, Javal keratometry and corneal topography
3. Measurement of tear production tests: Schirmer's or Zone Quick tests, fluorophotometry of the protein content in tears, osmolarity measurement, goblet cell density, tear mucus ferning pattern (TMFP), and lactoferrin microassays (3)

Korb showed in a study the importance of multiple tests in DES evaluation (10). The most frequently chosen tests by optometrists and ophthalmologists to

diagnose DES are (in order): dry eye questionnaire, TFBUT, fluorescein & rose bengal staining of the ocular surface and Schirmer's test. Schein showed in the Salisbury study that of the total participants, 2.2% were symptomatic and had a low Schirmer's test result ( $\leq 5$  mm), and 2% were symptomatic and had a high rose bengal test score ( $\geq 5$ ). Furthermore, 3.5% were symptomatic and had either a low Schirmer's score or a high rose bengal score, and 0.7% were symptomatic and had both a low Schirmer's score and a high rose bengal score. So there is minimal overlap between individuals identified by questionnaire, Schirmer tests, and Rose Bengal scoring (26 & 27).

### **Tear Mucus Ferning Patterns (TMFPs)**

TMFP evaluation, the objective method we used in our study, has many clinical applications. Fern crystallization of mucus was first described by the Romanian doctor, Papanicolau in the 1940's in samples from cervical mucus (21). In the ocular field, it has been demonstrated that mucus ferning patterns have a high specificity and sensitivity in the diagnosis of keratoconjunctivitis sicca, primary and secondary Sjogren syndrome (25, 32 & 14).

TMFPs are altered in patients with pinguecula (20), but not those with pterygium (4). This shows that alterations in the mucin layer may be a possible cause of pinguecula formation or that pinguecula causes an alteration in the mucin layer worsening DES. An alteration of the TMFP was also demonstrated in those with Down's syndrome and led to them having frequent infections of the anterior segment of the eye (5). TMFPs are altered after chronic application of commercially prepared formulations of timolol maleate (6). TMFP seem to be a good sensitive and specific predictor for contact lens tolerance in a clinical setting (23). Norn showed using his quantitative method, that the ferning area is significantly decreased in infectious conjunctivitis and after cataract extraction, possibly due to exudation from the conjunctival vessels (18). The TMFP does not show sex and age related differences in subjects, facts supported by Tabbara and Okumoto (31). TMFPs could be used together with other classic tests in diagnosing cystic fibrosis because altered electrolyte concentrations might be responsible for increased hyperviscosity of mucus in all body secretions (24). Exposure to draught in a car can improve the TMFP, due to increasing of the tears flow (33).

### **Ocular Surface Disease Index (OSDI)**

The OSDI is a valid and very specific questionnaire that measures ocular symptoms related to DES and its effect on daily life style. It has three subscales:

vision related function (6 questions), ocular symptoms (3 questions), and environmental triggers (3 questions) (28).

## **Current Study**

Our study has 3 goals:

1. Investigate any correlation between Tear Mucus Ferning Patterns (TMFPs) and the Ocular Surface Disease Index (OSDI) questionnaire
2. Assess if TMFPs can be used on a regular basis for DES diagnosis, especially in diagnosis of inner mucous layer deficiency since it is a simple, quick, and cheap clinical method
3. Point out the very important role of the optometric physician in the diagnosis, management and treatment of DES, and to adequately quantify the impact that dry eye has on quality of life on our patients

## **Fern Grading and Interpretation**

We classified ferning patterns according to the Rolando classification system, which is a qualitative method of classification, taking into consideration the integrity, uniformity, and branching of the ferning patterns. In this classification system, a type I pattern shows ferns in a uniform pattern with acute branching angles, without spaces between them. A type II pattern is similar to a type I, but it has some small empty spaces and a lower branching frequency. In a type III pattern, ferns are thicker and smaller, resembling a short armed right-angled cross with large spaces in between and little branching. In a type IV pattern tear mucus is poorly organized, ferns cannot be recognized or are barely present (25). Types I and II are seen in normal tears and types III and IV seen in abnormal tears.

Rolando's grading system has high reliability. Regarding the four-grade system, intra-observer agreement was found to be 85.41 %, and inter-observer agreement was found to be 80.62%. To simply separate normal (grades I and II) patterns from abnormal (grades III and IV) patterns, intra-observer agreement was found to be 94.50%, and inter-observer agreement 92.10% (21).

From published data, types I and II are found in >80% of normal eyes, while 90% of patients with keratoconjunctivitis sicca have types III and IV (9). Higher ferning grades are seen more frequently with increasing age (22).

Increased tear viscosity is caused by there being more by mucus than proteins in the tear film, even though both tear proteins and mucous glycoproteins have a



substantial effect on surface tension (8). Production of fern-like patterns depends upon a divalent/monovalent cation ratio, and on protein concentration. TMFPs can be progressively modified from type I to type II, III or IV by adding sodium chloride to normal tears. It can also be changed by adding tetracycline or ethylenediaminetetraacetic acid (EDTA), which selectively sequesters divalent ions. Addition of glucose alters the shape of the ferns, but retains their complexity. Addition of distilled water leaves no visible drying marks. Also, pure protein and glycoprotein dissolved in distilled water at concentrations similar to those in tears form no ferns (9).

Collecting tear film with a capillary tube gives the lowest coefficient of variation (6.4%) of collection methods, and the Rolando glass rod method gives the highest coefficient of variation (99-128%). Water instillation in the inferior fornix, and increased tear secretion do not alter the grade of ferning patterns. Mucomimetic substances, like methylcellulose, arachis oil, and expression of meibomian gland secretions in vivo reduce the amount of ferning. Norn showed that the fern phenomenon is not stained by alcian blue, rose bengal, fluorescein, lissamine green, or iodo-nitro-tetrazonium (19).

## **Materials and Methods**

We recruited 31 subjects (62 eyes) between the ages of 21 and 52 years old (average age of 25.28 years). They included 19 females and 12 males. 30 of the subjects were optometry students and one optometry faculty member. Our belief was that those who chose to participate in our study did so because they had DES (self assessment or had a previous diagnosis).

The study and procedures were fully explained; informed consent was then obtained from all subjects before proceeding with tear collection. The Institutional Review Board of Pacific University College of Optometry approved the protocol. Every patient underwent the following: filled out the OSDI questionnaire (subjective evaluation), allowed for tear collection and then had their mucus ferning patterns graded by taking photographs through a microscope (objective evaluation).

We used the OSDI scoring algorithm: 12 items on the OSDI questionnaire graded on a scale 0 to 4, (0, indicates no symptoms at any time; 1, some of the time; 2, half of the time; 3, most of the time and 4, all of the time). The total OSDI score was then calculated using the following formula:  $OSDI = [(sum\ of\ scores\ for\ all\ questions\ answered) \times 100] / [(total\ number\ of\ questions\ answered) \times 4]$ . Calculations were only

done after the TMFPs were graded to avoid any bias from the OSDI score being put into their grading.

TMFP testing involved the following:

1. Tear collection from the lower fornix of both eyes with a micropipette; no topical anesthetic was applied
2. Placement of the tear sample on a clean glass slide
3. Drying of tear sample at the room temperature for 5-7 minutes
4. Observation and photography of crystallized patterns under a microscope at 10x and 40x
5. Grading of ferning patterns according to the Rolando classification; patterns were agreed upon between two individuals

The grading patterns were then compared to the OSDI algorithm for any statistical significance and/or correlation.

## Results

Of the 31 subjects enrolled in our study, 28 had taken the OSDI questionnaire and had TMFP samples collected in the 1st session (October-November), and 27 of them had both in the 2<sup>nd</sup> session (April-May). So we had 55 total cases.

If there was a grading difference in the TMFPs between the two eyes, the worst grade was used in our analysis in the tables.

Based on OSDI algorithm scores, presented above, we classified the symptoms of our participants into three categories: severe scores  $\geq 29$ , moderate-mild scores 8-28, and normal scores 0-7. In a previous study, Schiffman & al found that normal subjects had an OSDI composite score of  $4.5 \pm 6.6$ , and that those participants scoring  $\geq 8$  are at least mildly symptomatic (29).

Table No. 1 analyzes the correlation between patient symptoms, given by the OSDI scores and TMFP grading for subjects in October-November 2003. 89.28% of our participants were symptomatic and 10.71% were not. From those with symptoms, 48% had an abnormal TMFP (grade III), and 52% had a normal TMFP (grades I or II). The 48% percent of those with abnormal patterns and symptoms is higher than any published data we found that compares subjective and objective tests in DES (26). Among those with no symptoms two of them had a normal TMFP (grade II), and one had a grade III.

Of those with symptoms, 36 % had severe symptoms, and 64% had moderate-mild symptoms. Among those participants with severe symptoms 44.44% had abnormal TMFP gradings. Among those with moderate-mild symptoms 50% had a grade III on TMFPs and 50% had normal patterns. One out of three or 33% of those with no symptoms had an abnormal TMFP.

Table No. 1:

1<sup>st</sup> session (October-November 2003) comparison of ODSI and TMFPs

ODSI Category/TMFP-Grade	I	II	III	IV	Total
Severe	1 (3.57%)	4 (14.29%)	4 (14.29%)	-	9 (32.14%)
Mild +Moderate	1 (3.57%)	7 (25%)	8 (28.57%)	-	16 (57.14%)
Total with symptoms	2 (8%)	11 (44%)	12 (48%)	-	25 (89.28%)
No symptoms	0 (0%)	2 (7.14%)	1 (3.57%)	-	3 (10.71%)
Total	2 (7.14%)	13 (46.43%)	13 (46.43%)		28 (100%)

There were 25 participants with symptoms and three without symptoms. Of the 25 with symptoms 12 had an abnormal TMFP.

Table 2 shows that in the 2<sup>nd</sup> session (April-May 2004), we had 22 participants (81.48%) with symptoms and five (18.52%) without symptoms. Of those with symptoms, eight (36.36%) had abnormal TMFPs, and 14 (63.63%) had normal ferning patterns.



Of the symptomatic participants 31.82% had severe symptoms and 68.18% had moderate-mild symptoms. Five of seven or 71.43% of participants with severe symptoms had an abnormal TMFP. Three of 15 or 20 % of participants with moderate-mild symptoms had an abnormal TMFP. On the other hand, only two of five or 40% of our participants without symptoms had a normal TMFP.

Table No. 2:

2<sup>nd</sup> session (April-May 2004) comparison of ODSI and TMFPs

ODSI Category/TMFP-grade	I	II	III	IV	Total
Severe	0 (0%)	2 (7.41%)	4 (14.81%)	1 (3.70%)	7 (25.93%)
Mild +Moderate	5 (18.52%)	7 (25.93%)	3 (11.11%)	-	15 (55.55%)
Total with symptoms	5 (22.73%)	9 (40.9%)	7 (31.82%)	1 (4.55%)	22 (81.48%)
No symptoms	0 (0%)	2 (7.41%)	3 (11.11%)	-	5 (18.52%)
Total	5 (18.52%)	11 (40.74%)	10 (37.04%)	1 (3.70%)	27 (100%)

There were 22 participants with symptoms and five without symptoms. Of the 22 with symptoms eight had an abnormal TMFP.

If we consider the 1<sup>st</sup> and 2<sup>nd</sup> sessions together, we had 55 total cases. 16 (29.1%) had severe symptoms, 31 (56.36%) had moderate-mild symptoms, and eight (14.55%) did not have any symptoms. Among those with severe symptoms, nine (56.25%) had an abnormal TMFP, and among those with moderate-mild symptoms 11 had an abnormal TMFP (35.48%). So of those with symptoms, 42.55% had an abnormal pattern. Among those without symptoms, four had a normal TMFP (50%).

Table No. 3:

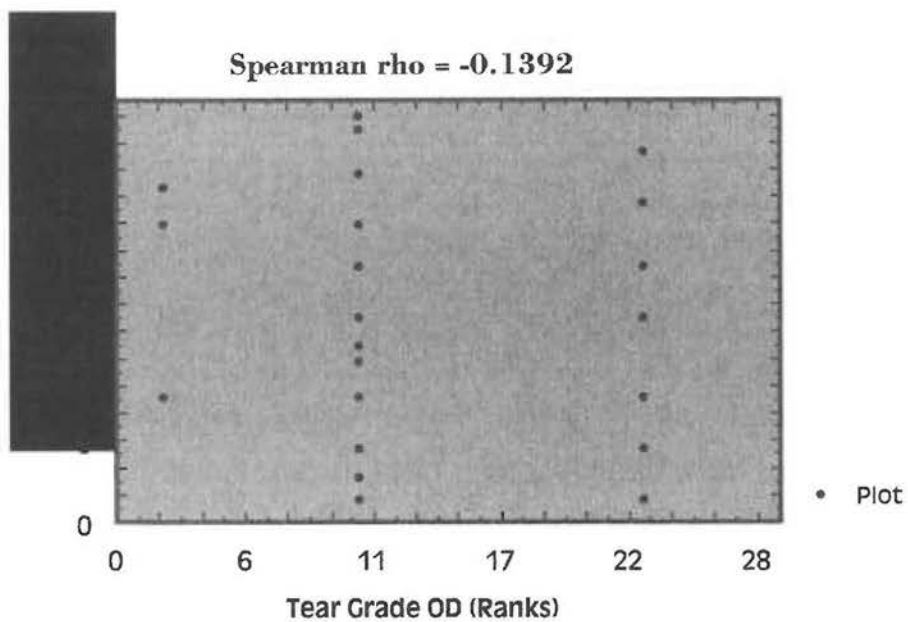
Both sessions (October-November 2003 & April-May 2004)

ODSI Category/TMFP-Grade	I	II	III	IV	Total
Severe	1 (1.82%)	6 (10.91%)	8 (14.55%)	1 (1.82%)	16 (29.09%)
Mild +Moderate	6 (10.91%)	14 (25.45%)	11 (20.00%)	-	31 (56.36%)
Total with symptoms	7 (12.72%)	20 (36.36%)	19 (34.54%)	1 (1.82%)	47 (85.45%)
No symptoms	0 (0%)	4(7.27%)	4(7.27%)	-	8(14.54%)
Total	7(12.73%)	24(43.64%)	23(41.82%)	1(1.82%)	55(100%)

There were 47 participants with symptoms and eight without symptoms. Of the 47 with symptoms 20 had an abnormal TMFP.

In our statistical analysis we used OSDI scores and right eye TMFP results. Due to the nature of the data, we used a conservative approach utilizing a rank test that is appropriate for ordinal, non-parametric data. This provides a correlation index (Spearman Rank Correlation). The r values we have are low-indicating a weak correlation. We have also included a comparison of the two administrations. The differences were not significant, as you can readily see by the plot and the calculated values. In summary, this shows that OSDI and TMFP are not predictive of one another.

Graph No. 1:



Sample Size: 28

Degrees of Freedom : 26

**Spearman rho: -0.1392**

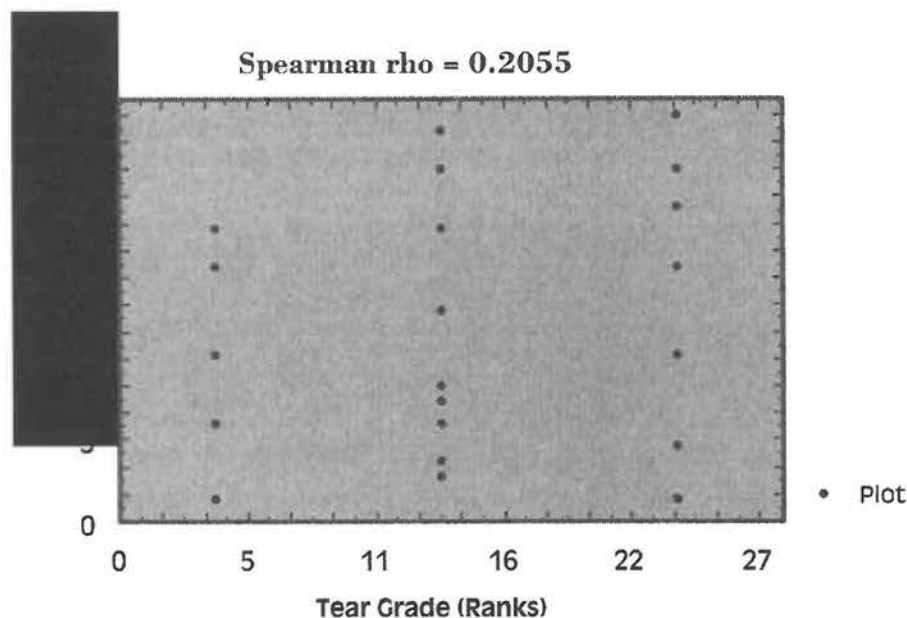
Test of Significance

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t-Value: -0.7168

2-Tail p: 0.4799

Graph No. 2:



Sample Size: 27

Degrees of Freedom : 25

Spearman rho: 0.2055

Test of Significance

t-Value: 1.0499

2-Tail p: 0.3038

Even though most patients that are symptomatic for DES don't have an abnormal TMFP, we found that 42.55% of subjects that were symptomatic had an abnormal pattern and this result is higher than any test we've researched that compares subjective symptoms to objective measurements. This shows that TMFPs should be used as one of the many tools in evaluating DES. It further shows that DES is a complex disease to diagnose and that it should still be diagnosed based on subjective symptoms rather than any specific objective test.

## Discussion

Since DES affects 3.63% of the USA population and over 4.3 million people older than 65 years of age have symptoms of dry eye disease, it is a very important condition that needs to be addressed by eye care professionals. Complications and symptoms may affect the quality of life of those with DES. There is not a standard dry eye questionnaire for DES diagnosis, but recently the most commonly used one is the OSDI.

Unfortunately, there is not one objective test that can be used to diagnose DES with much certainty. Also, it has not been demonstrated yet that there is any correlation or predictability between a patient's symptoms and any objective signs. Our study tried to explore the possibility of a correlation between the OSDI and TMFPs.

We decided to use the OSDI because it has been demonstrated to be a valid and specific test to measure ocular symptoms related to DES and its affects on daily lifestyle. It is also easily graded and allows for simple categorization of patients based on their symptoms (28).

The other test that we used in our study, TMFPs, has been utilized in different fields of medicine to demonstrate pathology or abnormalities of mucous cells in different secretions of the human body like tears, saliva, digestive juices and cervical secretions. Since it has been shown to be a good adjuvant test to demonstrate goblet cell pathology in conditions like Sjogren's syndrome and cystic fibrosis we elected to use it in our study. Finding a decreased amount of ferning (grades III or IV) is considered to demonstrate decreased amounts of the goblet cells at that specific anatomic level. As mentioned earlier, TMFP does not show differences between different genders and ages, supported by facts from Tabbara and Okumoto (31).

Rolando's system is the most commonly classification of TMFP because it is simple and quick. Even though it was demonstrated that there is a learning curve effect to its grading, Rolando's classification is easily able to separate normal from abnormal patterns (24 & 25).

To our knowledge this study is the first one to conduct research to find a correlation between the OSDI questionnaire and TMFPs. There are other studies that have compared a patient's symptomatology, using other methods than the OSDI questionnaire, with Schirmer's tests, tear film break up time and rose bengal vital

staining that didn't show a correlation between symptoms and objective signs (26 & 27). Also, OSDI was compared with Schirmer's test type 1, and 2, tear film break up time, and lissamine green vital staining without finding a strong correlation among them (28).

The method we used to collect the tears, capillary attraction with a calibrated micropipette, has a very low coefficient of variation (18). After the sample's collection, we let it dry for 5-7 minutes, took photographs of the most representative and significant parts of the sample under 10x and 40x magnifications, and then graded the photos later.

In the first session of testing, we found 25 out of 28 or 89.28% of our participants had symptoms (OSDI score of  $\geq 8$ ). 12 out of those 25 or 48% of them also had an abnormal TMFP (grade III). In the second session, 22 out of 27 or 81.48% of the participants had symptoms, and 8 out of those 22 or 36.36% had an abnormal TMFP (grades III and IV). Considering both sessions together, 47 out of 55 or 85.45 % of our participants had symptoms and 20 of those 47 or 42.55% had an abnormal TMFP.

In looking at the total number of subjects, 20 out of 55 or 36.36% were symptomatic and had an abnormal pattern. This number is high because our testing population was optometry students with self or previous doctor diagnosis of DES. It also explains the very high number of subjects that were symptomatic. In the optometry student population there is a higher incidence of DES because of a higher prevalence of contact lens wearers and those that have had LASIK surgery. In our cohort, we had 15 contact lens wearers, one had LASIK done previously, one was pregnant and one was breastfeeding. All of those factors have been recognized as a DES etiology.

Taking in consideration each case individually, statistical analysis provides a correlation index (Spearman Rank Correlation) very low,  $r$  number being -0.1392 for the 1<sup>st</sup> session, and 0.2055, for the 2<sup>nd</sup> session. This indicates a very low correlation between OSDI and TMFPs. This result is consistent with previous studies that could not find a strong correlation between the objective clinical signs and patient symptomatology. This also correlates with the fact that when eye care practitioners were asked to identify a single objective test that is the most important for DES classification and diagnosis, they were unable to mention the same one. Most use several objective tests to aid in DES evaluation (10). However, they do agree that the dry eye questionnaire, a subjective test, is the main tool in DES classification and diagnosis.

Even though TMFPs cannot be used as a single objective test for DES diagnosis, we want to point out that the main indication for using the TMFP test is when there is a suspicion of a mucus deficiency in tears. This could be a starting point for more research in this area.

Also, we believe that our patients should find out about symptoms and management of DES from their eye care professionals, rather than from the media as discussed earlier in the study.

In conclusion, TMFPs should be used as an adjuvant test in evaluating DES because it is very quick, simple, valid and reliable. It shouldn't only be used by eye care practitioners, but also by other medical specialists like primary care practitioners, rheumatologists, etc...



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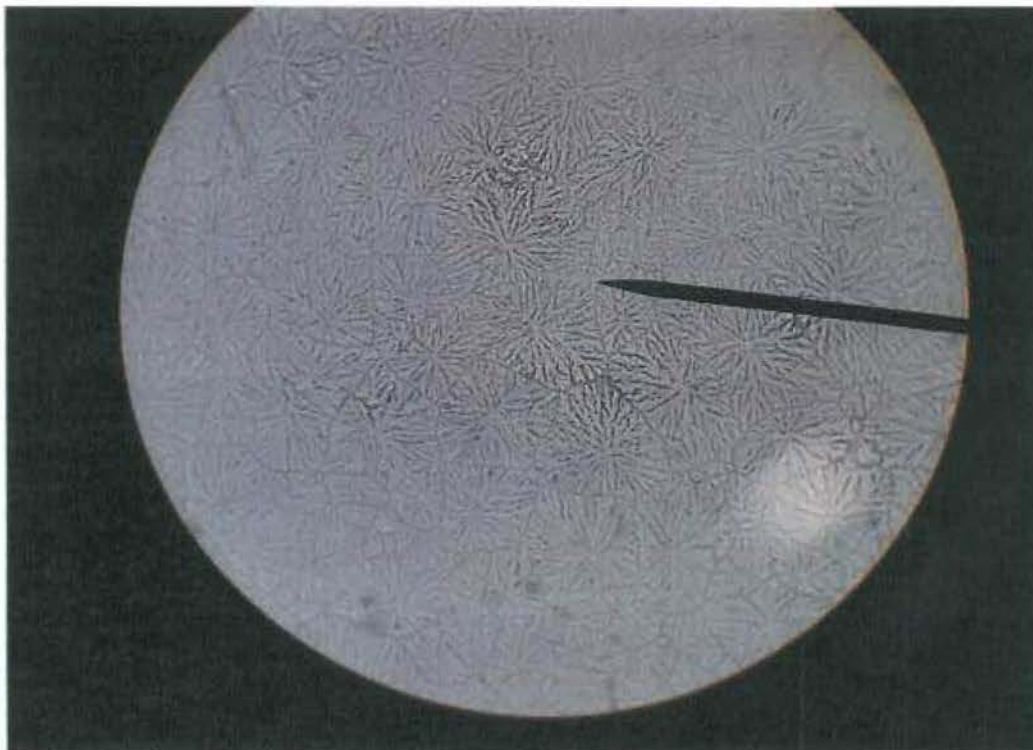
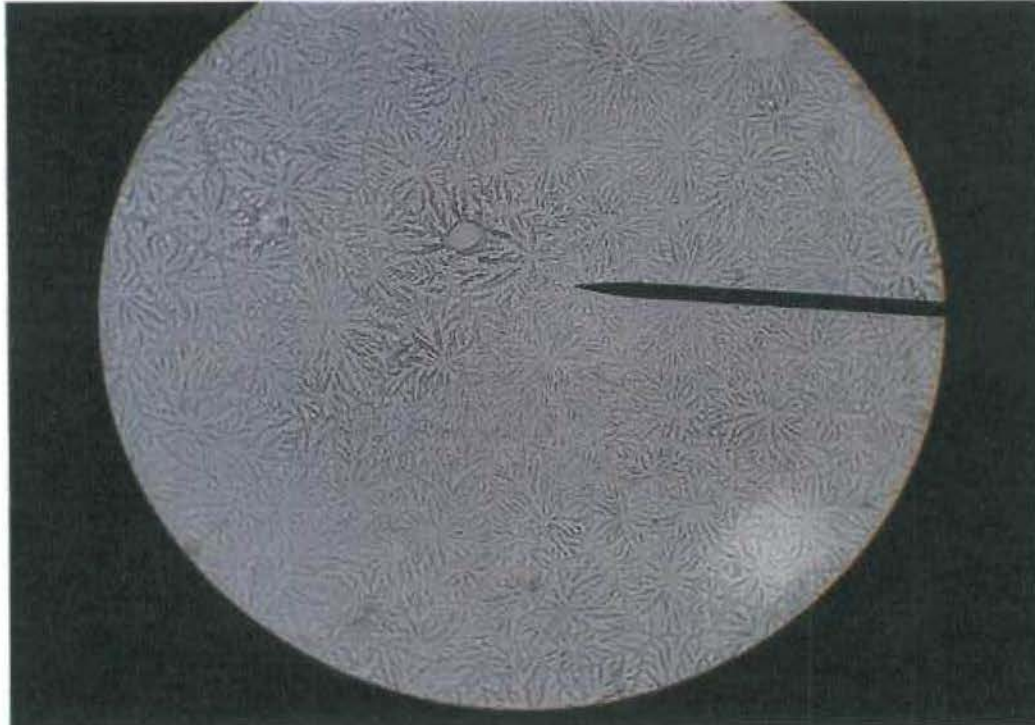


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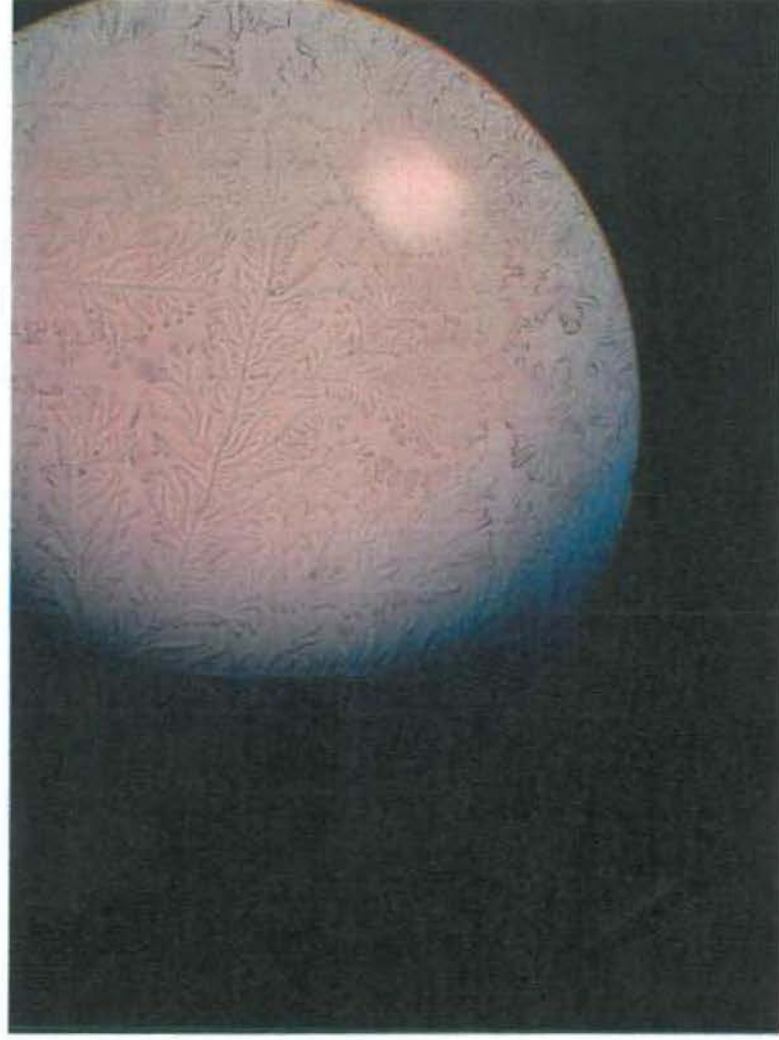
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**TEAR MUCUS FERNING PATTERN - Rolando qualitative classification:**

Grade I of TMFP:

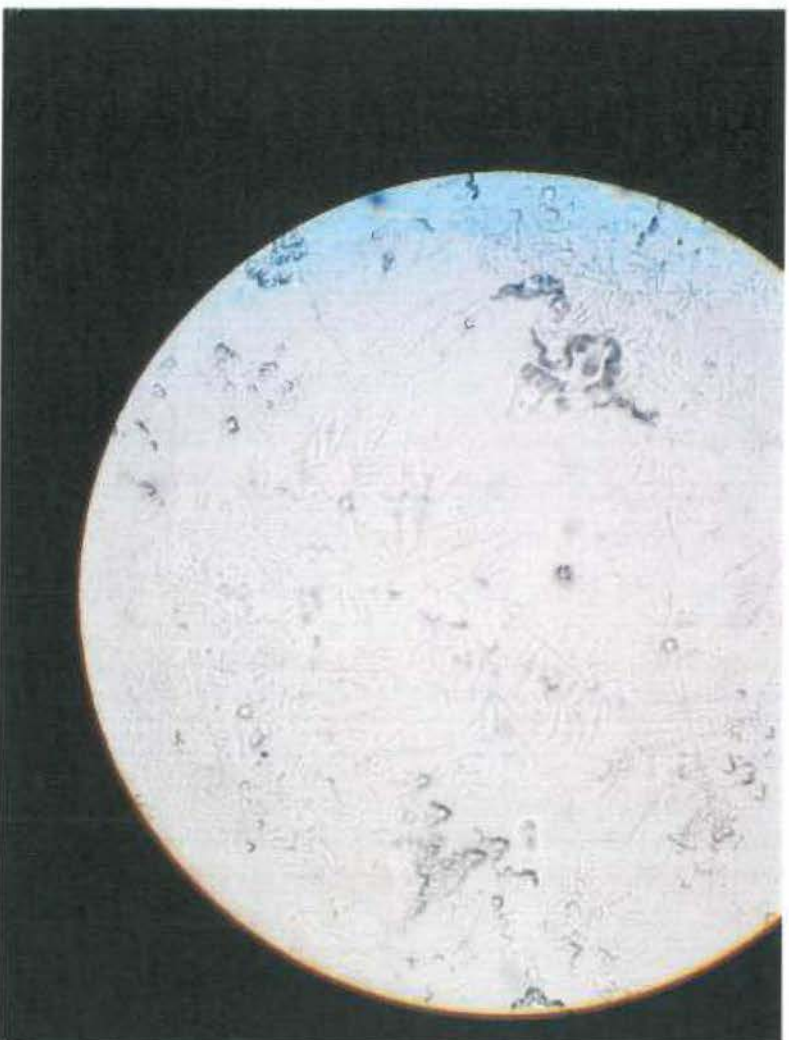
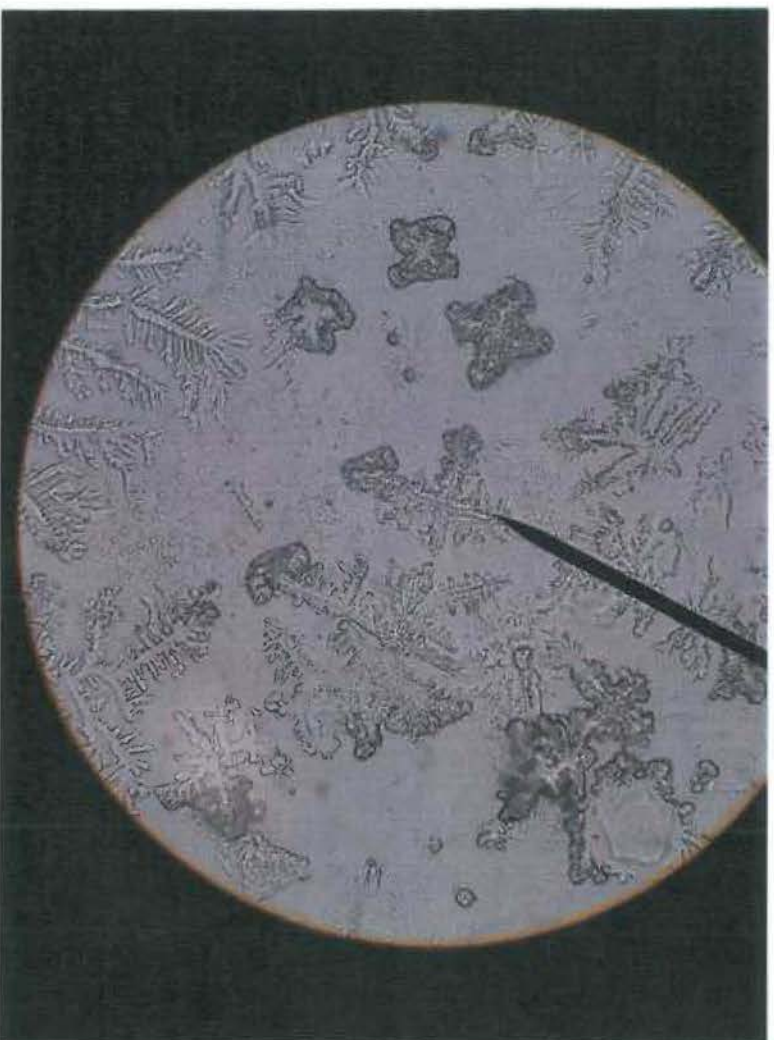


Grade II of TMFP:





Grade III of TMFP:



Grade IV of TMFP:

